In vivo Performance of Combinations of Autograft, Demineralized Bone Matrix, and Tricalcium Phosphate in a Rabbit Femoral Defect Model

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Statement of Purpose: Regeneration of bone gap defects due to trauma, injury, or tumor resection can be accomplished by transplantation of either autografts or allografts.[1] Autografts have been considered the gold standard; they fulfill specific healing criteria of osteogenesis, osteoinduction, and osteoconduction. Due to the limited availability of autograft tissue and donor-site morbidity, tissue engineering-based products such as bone graft substitutes. A readily available and clinically viable strategy to enhance the osteogenic capacity of synthetic bone grafts is to incorporate autografts and/or allografts into substitutes. Therefore, the primary purpose of the present study was to determine the *in vivo* performance (biocompatibility and bone healing response) of different combinations of synthetic bone graft substitute (BGS), demineralized bone matrix (DBM), and particulate bone autograft (PBA) in a rabbit distal femur defect model. A commercially available TCP-based synthetic BGS was chosen as a synthetic bone substitute (*e.g.*, ChronOS).

Methods: Commercially available synthetic bone graft materials and DBM were supplied by Synthes USA (West Chester, PA). The DBM was comprised of rabbit demineralized bone in a sodium hyaluronate carrier. PBA was harvested from the posterior iliac crest. Bilateral unicortical femoral defects were surgically prepared and treated with combinatorial bone grafts according to one of 7 treatment groups. Recipient sites were retrieved at 6 weeks. Cellular/tissue responses and new bone formation in the defects were determined at 6 weeks post-implantation using histology and histomorphometry.

Results: Histology images revealed that new bone formation was apparent inside all defects when treated with combinations of PBA, DBM, and BGS. Higher magnification (5×) revealed details of new bone formation inside defects (**Fig. 1**). Cancellous bone regeneration (blue staining) was clearly observed in the defect area with excellent host bone integration of PBA or integration of newly formed bone (blue staining) with remaining materials, either DBM or BGS (black/grey). One of the interesting findings was that BGS-containing groups (BGS alone as well as BGS mixtures with DBM) performed similar to the allograft (*i.e.*, DBM) in terms of new bone formation quantity. This is noteworthy in that allografts such as DBM are known to have better osteogenic capacity than most synthetic bone grafts. Furthermore, although autografts and/or allografts are still a popular clinical choice for bone regeneration, synthetic alternatives to natural grafts will benefit patients due to the growing concerns of safety and cost-efficiency.[2] Overall, there appeared to be no detectable adverse tissue responses such as inflammatory or immune reactions (e.g., macrophages, lymphocytes, or foreign body giant cells), osteolysis in the recipients treated with combinations of PBA, DBM, and/or BGS. The materials (*i.e.*, DBM and BGS) appeared to form a compatible bone–implant interface (*i.e.*, no connective tissue interface between host bone and implants).

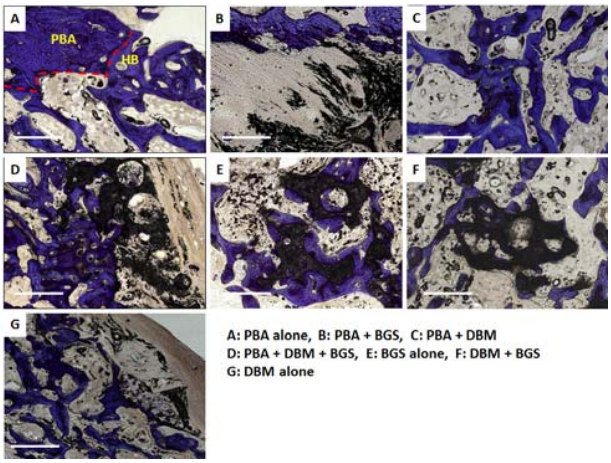

Figure 1. Representative histology images (5x) showing detailed bone healing response to different implants at 6 weeks post-implantation. Cancellous bone regeneration (blue staining) was clearly observed in the defect area with excellent host bone integration of PBA. All specimens are seen cut in the axial plane. Bone can be identified by blue staining. Black/grey indicates remaining implants in the defects. Scale bar = 200 μm.

Conclusions: Combinations of autografts (*i.e.*, PBA), allografts (*i.e.*, DBM), and a synthetic bone graft based on TCP appear to promote osteointegration. No adverse effects such as inflammatory reactions or osteolysis (*e.g.*, bone resorption) in a rabbit femoral defect model were observed over the course of the study. Histology and histomorphometry revealed that the synthetic bone graft substitute promoted new bone formation comparable to that by the allograft. These data suggest that synthetic BGS has potential as an alternative to allografts, thus preventing complications associated with allografts, such as disease transmission.

References:

1. Khan Y, et. al., JBJS-Am. 2008;90A:36-42.
2. Carragee EJ, et. al., Spine J. 2011, 11:471-91.